

**REMARKS**

**Regarding the Amendments**

No claims are amended by the present response. As pending, the claims are supported by the specification and the original claims. Thus, upon entry of the Response, claims 2 and 3 are canceled, claims 1 and 4 to 53 will be pending.

**Rejection Under 35 U.S.C. §103**

Claims 1 and 4 to 53 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Evans in view of Tseng, Woodward, Clark, Hoffman, Krall, Almen, EP 0 747 069, Leung, McIntire and Berger. Applicants respectfully traverse the rejection.

It is stated in the present Office Action that Applicants' previously presented arguments have been considered, but are deemed unpersuasive. Specifically, it is alleged that McIntire teaches that polymers of alkyl cyanoacrylates may be added to monomer alky cyanoacrylates to prevent undue escape of the adhesive from any given area and to allow sufficient time for the monomeric material to polymerize. It is also alleged that Berger teaches the use of two different monomers which provides enhanced flexibility of the polymer, and that with the previously cited references, the collection of eleven cited references teach the claimed invention. Applicants respectfully disagree.

In order for an invention to be *prima facie* obvious under MPEP § 2142, three requirements must be met: 1) there must be some suggestion or motivation to combine or modify the reference teachings; 2) there must be a reasonable expectation of success; and 3) the combined prior art references must teach or suggest all of the claim limitations. As discussed in detail below, the requisite motivation to combine is lacking, there would not have been a reasonable expectation of success if the motivation to combine had been present, and the prior art does not teach or suggest all

of the claim limitations of the invention. Therefore, Applicants respectfully submit the claimed invention is not *prima facie* obvious.

**1. Combined Prior Art Must Teach or Suggest All of the Claim Limitations**

It is respectfully submitted that these eleven references taken together do not teach or suggest all of the elements of the claimed invention. Independent claims 1, 24, 27, 38 and 46 recite a composition or the use thereof. As discussed above, the composition of these claims polymerizes upon contact with an anionic environment and contains two components, where the first component includes at least two polymerizable alkyl cyanoacrylate monomers and the second component includes an oligomer. The second component contains an oligomer of polymerizable alkyl cyanoacrylate monomer, a plasticizer, and an opacifying agent. None of the cited references, alone or in combination teach or suggest such a composition or its use and therefore cannot anticipate the claimed invention.

Evans does not teach or suggest all of the elements of the present invention. While Evans discloses treatment of arteriovenous malformations employing a biocompatible prepolymer, such as a cyanoacrylate, Evans does not teach or suggest use of more than one cyanoacrylate, nor does Evans teach a second component containing a cyanoacrylate oligomer. The claimed invention recites a combination of a first and second component. It is noted that the first component must contain a minimum of at least two polymerizable alkyl cyanoacrylate monomers. Additionally, the plasticizer of the second component serves to render the resulting polymer of the invention flexible (see, for example, page 16 of the specification). Such flexibility allows placement of the compositions and inhibition of breakage of the polymer to smaller pieces, that may enter the bloodstream and cause a catastrophic event. In addition to not teaching all of the claim elements, Evans contains no suggestion or motivation to further combine the single cyanoacrylate with another or with a second component, including any of the elements: an oligomer of a polymerizable alkyl cyanoacrylate monomer, a plasticizer, or an opacifying agent. As Evans does not teach or suggest all of the

elements of the present invention, nor does it suggest combination of its teachings with additional elements, it is respectfully submitted that the present invention is not obvious in light of Evans. Evans, even viewed in light of Tseng, Woodward, Clark, Hoffman, Krall, Almen, EP 0 747 069, Leung, McIntire and/or Berger still do not teach or suggest all of the elements of the claimed invention.

The Examiner acknowledges that the prior art does not expressly disclose the use of mixtures of alkyl cyanoacrylates with a second component which includes an oligomer of alkyl cyanoacrylate, a plasticizer and opacificant agent. McIntire is cited in the Office Action as teaching that polymers of alkyl cyanoacrylates may be added to monomer alkyl cyanoacrylates to prevent undue escape of the adhesive from any given area and to allow sufficient time for the monomeric material to polymerize. Berger is also cited as teaching the use of two different monomers which provides enhanced flexibility of the polymer, and therefore it is alleged that in combination with the teachings of Evans and the other cited references, McIntire and Berger render the claimed invention obvious. Applicants respectfully disagree.

McIntire teaches a specific method of making poly( $\alpha$ -cyanoacrylates), which may then be used as viscosity modifiers. However, McIntire is not the first to use poly( $\alpha$ -cyanoacrylates) as viscosity modifiers. It is stated in col. 2, lines 34-40 that the poly( $\alpha$ -cyanoacrylates) prepared by the method of McIntire could be added in smaller amounts than "prior art poly( $\alpha$ -cyanoacrylates)" to achieve the same viscosity effects. Therefore, poly( $\alpha$ -cyanoacrylates) as viscosity modifiers were already known in the art. The background section of McIntire discusses use of poly( $\alpha$ -cyanoacrylates) and states that there is a need in the art for viscosity modifiers to be added to "the monomeric material [the  $\alpha$ -cyanoacrylate]" (col. 1, lines 62-63). However, the teaching of a method of making a single viscosity modifier does not obviate the claimed invention. In the reference there is no teaching or suggestion of an adhesive composition comprising more than one cyanoacrylate monomer, nor combination with a plasticizer and an opacifying agent. Therefore, McIntire, taken in combination with the other cited references, does not teach or suggest the composition of the claimed invention.

Similarly, it is respectfully submitted that Berger, taken in combination with the other cited references, does not teach all of the elements of the claimed invention. Berger does not teach addition of any two cyanoacrylate monomers to increase flexibility, but teaches specifically addition of a C<sub>10</sub>-C<sub>12</sub> alkyl cyanoacrylate ester to a C<sub>1</sub>-C<sub>8</sub> alkyl cyanoacrylate ester to form a flexible cyanoacrylate polymer, which is preferably flexible enough not to need a plasticizer. The claimed invention, however, teaches use of the combination of monomers, preferably with different alkyl side chains, in order to modify the characteristics of the resulting polymer (for example, polymerization rate and/or flexibility) to what is optimal for a desired application (see, for example, page 16 of the specification) and teaches the component in conjunction with a second component, containing a plasticizer. As Berger is directed to optimizing flexibility while minimizing plasticizer use, Berger teaches away from the claimed invention. One of skill in the art would not be motivated to combine the teachings of Berger with the other references to obtain the claimed invention.

Tseng does not teach or suggest all of the elements of the present invention. Specifically, Tseng discusses 2-cyanoacrylates widely used in surgical fields, however one of skill in the art would not be motivated by the teachings of Tseng to combine these 2-cyanoacrylates with any other cyanoacrylates. Tseng does not teach or suggest the combined use of multiple cyanoacrylates in a composition or addition of a second component comprised of an oligomer of a polymerizable alkyl cyanoacrylate monomer, a plasticizer, and an opacifying agent.

Similarly, Woodward does not teach or suggest all of the elements of the present invention. While Woodward discloses hexyl 2-cyanoacrylate and evaluates its properties in vivo, one of skill in the art would not be motivated by the teachings of Woodward to combine these hexyl 2-cyanoacrylates with any other cyanoacrylates. Woodward does not teach or suggest the combination of the present invention.

Also cited as rendering the claimed invention obvious, when viewed with McIntire, Berger, Evans, Tseng and Woodward are Clark, Hoffman, Krall, Almen, EP 0 747 069 and Leung.

Applicants respectfully submit that there is no motivation to combine these references and that the teachings of the cited references do not disclose all of the elements of the claimed invention and therefore the claimed invention is not obvious in light of the references. Specifically, none of Clark, Hoffman, Krall, Almen, EP 0 747 069 and Leung teach or suggest a composition of two components, where the first component contains at least two polymerizable alkyl cyanoacrylates and the second component contains an oligomer of an alkyl cyanoacrylate monomer, a plasticizer and an opacifying agent.

Clark was previously cited as discussing that plasticizers give cyanoacrylates flexibility and that stabilizing agents may be added to inhibit polymerization. It is respectfully submitted, however, that these are characteristics well known in the art, as may be seen in the Background of the Clark reference. As can be seen in col. 2, lines 11 to 39 of Clark, the characteristics of plasticizers and stabilizing agents were well known in the art prior to the filing of Clark. However, even if one of skill in the art used plasticizers or stabilizing agents with cyanoacrylates, the teachings of Clark would not motivate one of skill in the art to combine a plasticizer and stabilizing agent in a two component composition, where the first component contains at least two polymerizable alkyl cyanoacrylates and the second component contains an oligomer of a alkyl cyanoacrylate monomer, a plasticizer and an opacifying agent, such as that in the claimed invention.

Hoffman was also previously cited as allegedly to rendering the present invention obvious, when viewed in light of the other cited references. It is not clear, however, what Hoffman is relied upon to show, as Hoffman, while cited, is not discussed substantively the Office Action mailed September 9, 2003, the Office Action mailed March 26, 2003, or the Office Action mailed October 22, 2003. It is assumed that Hoffman, like Krall, is cited as teaching a method of female sterilization comprising administration of cyanoacrylates. It is Applicants' position that the claimed invention is not obvious in light of Hoffman, as Hoffman, even when viewed in light of the cited references, does not teach or suggest all elements of the claimed invention.

Specifically, Hoffman teaches a method of sterilization utilizing a cyanoacrylate, but in the teachings of Hoffman the cyanoacrylate is administered to induce an inflammatory response and encourage the growth of scar tissue, which results in subsequent blockage of the fallopian tubes. In fact, Hoffman teaches away from the composition of the claimed invention and use of the same, in that use of a composition in the method of Hoffman will degrade after it is administered and has served its function (see col. 1, lines 47 to 62). In addition, Hoffman does not describe a composition that includes a second component containing an oligomer of a polymerizable alkyl cyanoacrylate monomer, a plasticizer, and an opacifying agent. Therefore the composition of the claimed invention is not obvious in light of Hoffman, nor is the composition obvious in view of Hoffman in combination with the other cited references.

Similarly, though Almen describes alkyl cyanoacrylates as a good adhesive compromise, and Leung describes alpha cyanoacrylates as good adhesives, neither reference, alone or in combination with the other cited references teaches or suggests the combination of components of the claimed invention. One of skill in the art would not be motivated by the teachings of Almen and/or Leung to develop the claimed combination of two components. While alpha cyanoacrylates are described by Almen and Leung as being good adhesives, there is no teaching or suggestion of utilizing a first component containing at least two polymerizable alkyl cyanoacrylate monomers and a second component containing an oligomer of a polymerizable cyanoacrylate monomer to obtain an optimum composition. Therefore the composition of the claimed invention is not obvious in light of Almen and/or Leung in combination with the other cited references.

In addition, EP 0747069 does not teach or suggest all of the elements of the present invention. Though EP 0747069 describes a medical device for administering compounds like cyanoacrylates, when the teachings of EP 0747069 are taken in combination with the other cited references, it does not teach or suggest administration of the claimed compound, as the combination of references does not teach or suggest the claimed compound itself. Accordingly, the claimed methods of the invention

including administration cannot be obvious in light of the combination of EP 0747069 with any or all of the other cited references.

As the cited references do not suggest or motivate a combination of their teachings, one of skill in the art would not have reasonably expected the combination of references to produce a useful composition. Additionally, because all of the cited references, taken together do not teach or suggest all of the elements of the claimed invention, it is respectfully submitted that Evans in view of Tseng, Woodward, Clark, Hoffman, Krall, Almen, EP 0 747 069, Leung, McIntire and Berger does not anticipate the claimed invention under 35 U.S.C § 103(a). Withdrawal of the rejection is therefore respectfully requested.

## **2. Reasonable Expectation of Success**

It is respectfully submitted that, although there is no suggestion or motivation to combine Evans with Tseng, Woodward, Clark, Hoffman, Krall, Almen, EP 0 747 069, Leung, McIntire and/or Berger, even if there were such a suggestion or motivation to combine, there would not have been any reasonable expectation of success in any such combination.

Reasonable expectation of success is measured at the time of invention. It is stated in MPEP§ 2141.01(III) that a rejection of claims under 35 U.S.C §103 must be made without the benefit of hindsight afforded by the claimed invention. It is respectfully submitted that the present rejection for obviousness is based on improper hindsight. It is Applicants' assertion that one of skill in the art would not have selected the eleven cited references ranging from 1968 to 1997 from all the references regarding cyanoacrylates to assemble the claimed invention without the benefit of the teachings of the claimed invention. In this respect, one of skill in the art would not have had a reasonable expectation of success in the combination of two components, the first including at least two polymerizable alkyl cyanoacrylate monomers and the second including an oligomer of a polymerizable alkyl

cyanoacrylate monomer, a plasticizer and an opacifying agent, where the composition would polymerize upon contact with an anionic environment.

Accordingly, Applicants maintain that inventive steps were required, which would not have been obvious to those skilled in the art, to obtain the claimed composition and the methods of utilizing the same.

### **3. Suggestion to Combine or Modify the Reference Teachings**

The Office Action alleges that the prior art does provide a motivation to combine the references, for example the desirability of mixtures of different cyanoacrylates and the use of plasticizers, opacifying agents, as well as the use of the compositions to occlude body passages, vessels, cavities. Additionally, it is further stated that Applicants have argued against the references individually, and that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references (citing *In re Keller*).

Applicants respectfully submit there is no suggestion or motivation to combine Evans with Tseng, Woodward, Clark, Hoffman, Krall, Almen, EP 0 747 069, Leung, McIntire and/or Berger. Each reference was discussed both individually and in combination with the other cited references in the prior responses. In addition, the cited references are discussed in combination in the present response.

The Office Action further cites *Keller* in stating that the test for obviousness is what the combined teachings of the references would have suggested to those of ordinary skill in the art. Applicants respectfully submit that the combined references do not expressly or even implicitly teach or suggest the claimed invention.



Finally, it is stated in the Office Action that the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references. Applicants respectfully submit that a *prima facie* case of obviousness has not been made.

The present invention discloses a combination of a first component containing at least two polymerizable alkyl cyanoacrylate monomers (selected from methyl cyanoacrylate, 2-hexyl cyanoacrylate, and others recited in claim 5) and a second component containing an oligomer of a polymerizable alkyl cyanoacrylate monomer, a plasticizer, and an opacifying agent. In addition, the present invention further discloses that the monomer component include a polymerization inhibitor. This polymerization inhibitor serves to inhibit breakage of the polymer. The opacifying agent acts to selectively absorb or deflect radiation, making the material visible under x-ray or any similar imaging technique. The composition of the claimed invention polymerizes upon contact with an anionic environment. None of the cited references, alone or in combination teach or suggest such a composition or its use and therefore cannot anticipate the claimed invention. In addition, none of the cited references teach or suggest the use of 2-hexyl cyanoacrylate, one of the monomers used in the first component of the claimed invention. For the reasons discussed above, Applicants respectfully submit that a case of *prima facie* obvious has not been established. Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. 103(a).

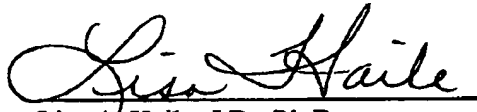
**CONCLUSION**

In summary, for the reasons set forth herein, Applicants maintain that claims 1 and 4-53 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at the number listed below. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

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